Direct Electronic Sensing of Biomolecular Activity and Signaling

NSF NIRT Grant 0404057

PIs: **Philip Collins, Reg Penner, Gregory Weiss, Nancy Allbritton**
University of California at Irvine

[Instructions: Introduce the research area and project objectives. Discuss methods employed, field of impact, collaborations and notable results. Write for an audience of diverse NSE grantees and the wider scientific research community. (At a level roughly equivalent to that of a article in the journal Science.) Use text and figures as appropriate. It is important to include contact information, links, and important references at the end as shown below.]

The primary goal of this research program is to develop hybrid bioelectronic devices with single-molecule sensitivity. Using an architecture based upon nanoscale conductors directly wired into circuits, these devices may provide new routes for both fundamental and applied nanoscience. The research team aims to fabricate and test biofunctional circuits, and then apply their use to explore enzymatic activity and biomolecular dynamics at the single molecule limit.

Figure 1 below schematically depicts a hypothetical single-molecule sensor and captures the promise of different types of science which might be investigated. First, a biomolecule like calmodulin is covalently attached to a nanocircuit (Fig. 1a). Various dynamics of the biomolecule are then electronically monitored, as depicted in Figs. 1b-d. The UCI research team combines a range of interdisciplinary expertise in nanocircuit assembly and testing, the electronic behaviors of circuits in electrolytes, phage display of target and receptor proteins, and the biological interdependence of kinase proteins and their substrates.

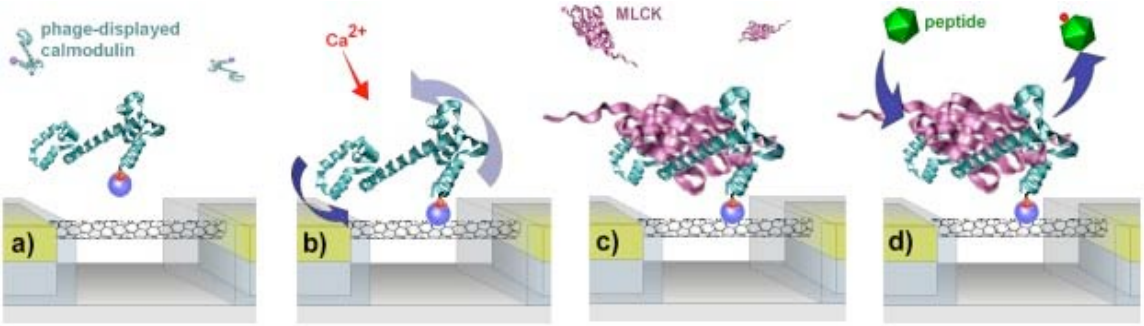

Figure 1. Schematic of a hybrid bioelectronic device

During the first year of this NIRT project, three different circuit architectures have been pursued in parallel. In one architecture, biological phage is used as the interconnecting "nanowire" and the phage conductivity is directly monitored as phage-displayed proteins interact with their surrounding environment. In a second architecture, a hybrid phage/Au electrode is fabricated on a quartz crystal microbalance for simultaneous electrical and mechanical interrogation. In the third architecture, proteins have been covalently bound to carbon nanotube circuits by electrochemically producing and tailoring defect sites in the nanotube sidewall.

Figure 2 depicts a phage nanocircuit in which two gold electrodes (vertical stripes) are bridged by many phage. The devices are electrically characterized using a small, 30mV alternating bias over a frequency range of 0.1 to 10^6 Hz. While the real part of the device impedance is not particularly sensitive to binding events on the phage, antibody binding events result in a major increase in the capacitive, imaginary part of the impedance [2]. We find that either the signal-to-noise (S/N) ratio of the imaginary component or the impedance phase angle can be used to identify electrical signatures of the binding. Using appropriately-labeled antibodies the electrical signals can be correlated with fluorescence images.

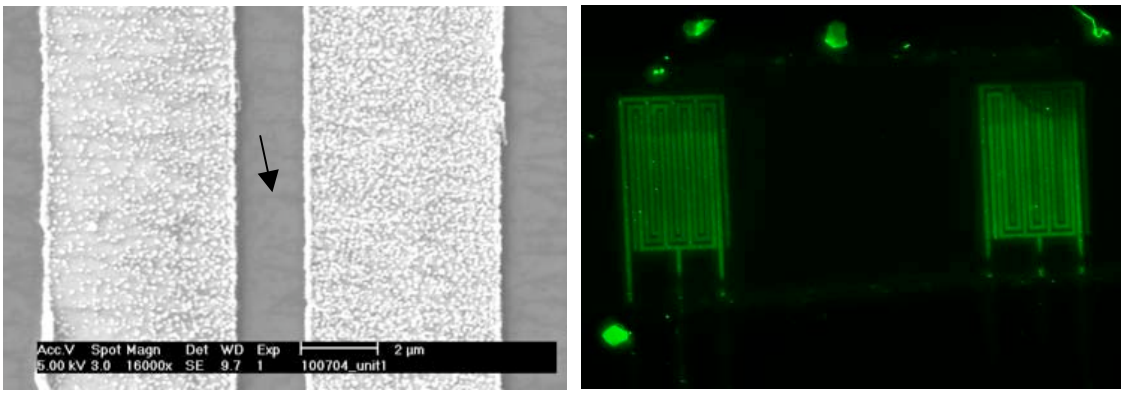

Figure 2. Electrically-connected phage nanocircuits, before and after binding of fluorescently-labeled antibodies.

Figure 3 depicts the carbon nanotube architecture following electrochemical modifications [3]. In this case, a nanotube provides a conducting pathway through the device. One or more defect sites on the nanotube provide chemically reactive sites to which different receptor molecules may be attached. The image at right depicts individual, single-walled carbon nanotubes to which a single label (top) and multiple labels (bottom) have been attached. The nanotube circuits, which behave like field-effect transistors, can be electronically monitored before, during, and after chemical attachments are made.

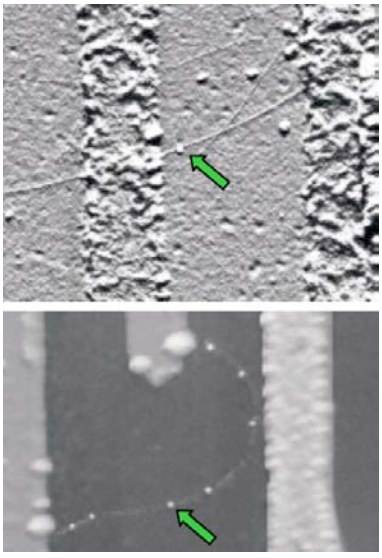

Figure 3. Carbon nanotube circuits having individual chemical attachment sites.

The research team has developed and verified different reaction protocols for tailoring these sites with different proteins. A common attachment reaction to carboxyl groups is via amide bond formation. Reaction conditions have been modified from both surface plasmon resonance studies using attachment to carboxylate coated surfaces and from the literature describing reactions with carbon nanotubes in solution. The number of attached sites is typically too low for optical spectroscopies, so the characterization of the attachment yield has required

development of alternate methods. The yield is currently measured using two complementary methods -- fluorescence and enzyme substrate turnover. The latter method has proven particularly useful in optimizing reaction conditions.

References

[1] For further information about this project link to **www.physics.uci.edu/~collinsp/** or email **collinsp@uci.edu**
[2] L.C. Yang, P.Y. Tam, B.J. Murray, T.M. McIntire, G.A. Weiss and R.M. Penner, "Virus Electrodes for Universal Biodetection", Nature-Chemical Biology, submitted.
[3] Y. Fan, B. Goldsmith and P. G. Collins, "Identifying and counting point defects in carbon nanotubes," *Nature Materials* **4** (2005).